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SynBio

Corporate Overview
September 2025

In vivo engineering for disease treatment and prevention

Developing Transformative Medicines for People with Cancer

Esphera SynBio is a synthetic biology company deploying the **ExoGen platform** for the in vivo generation of medicines

Differentiated and De-Risked Lead Asset

- Extensive CMC and clinical experience

High Potential Platform/Pipeline with Active Pharma Engagement

- Active Pharma collaboration (LNP/mRNA vaccines)
- In vivo CAR-T asset
- Non-dilutive engine to fund pipeline

Experienced Team

- 5 companies founded; 5-company exits
- >$500M non-dilutive financing
- 17 trials, 26 patents, 226 papers

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Introducing ExoGen Platform: Engineering Medicines In Vivo

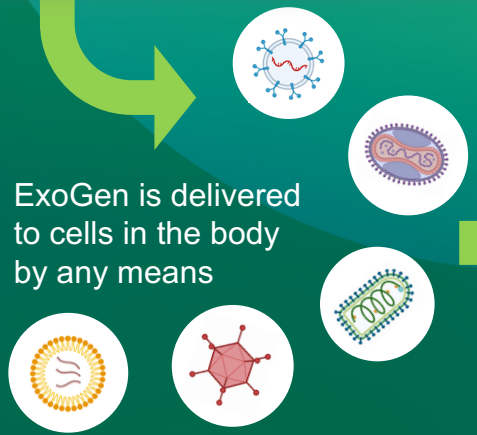
Synthetic nucleic acid transgene encoding a multimeric fusion protein designed to traffic to budding vesicles

Extravesicular Targeting Domain

Synthetic TMD to enrich fusion protein in budding vesicles

Luminal Cargo Domain

ExoGen is delivered to cells in the body by any means



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ExoGen Design for Oncology Lead Asset ESPH-01

Nanomedicine targeting:
Immune cells (ScFv)

Payload delivered:
STING agonist

Extravesicular Targeting Domain

Lead Oncology Asset:

- Proprietary ScFv targeting human and murine DEC205
- Delivering antigens to dendritic cells to enhance antigen presentation

Synthetic Transmembrane Domain (TMD)

Core Esphera Technology:

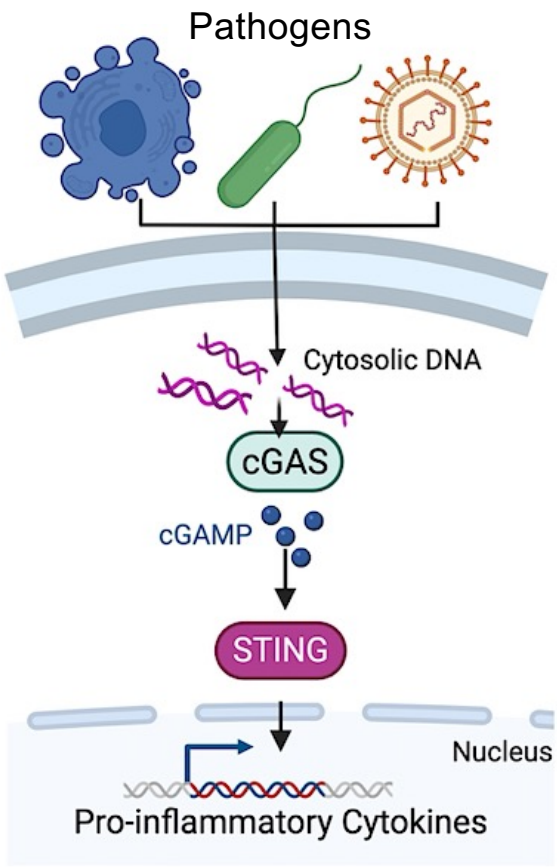
- Artificial and proprietary
- Superior for vesicle loading

Luminal Cargo Domain

Proprietary Immunostimulatory Enzymes:

- Bacterial dinucleotide cyclases constitutively generate cyclic dinucleotides: potent STING agonists

Functional STING pathway



First generation approaches to agonize STING have failed

Our understanding of STING biology has evolved:

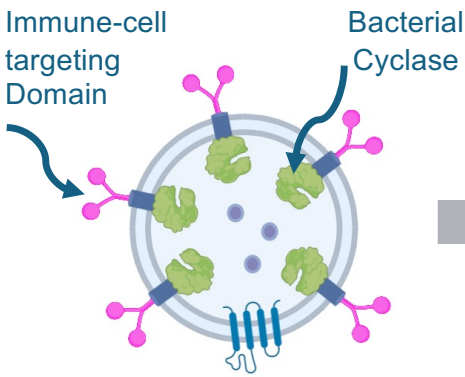
1. Targeting cancer cells with small molecule STING agonists in attempts to turn ‘cold tumors hot’ doesn’t work well; most cancers have evolved defects in their STING signaling

2. Delivery of STING agonists leads to off-target effects: STING activation in effector immune cells (T-Cells, B-cells) is extremely toxic

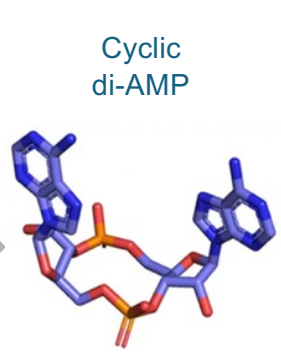
The solution to STING agonism is targeted delivery to antigen presenting cells to generate potent anti-tumor immune responses

STING Potential Unlocked: ExoGen Solution for Precision Activation

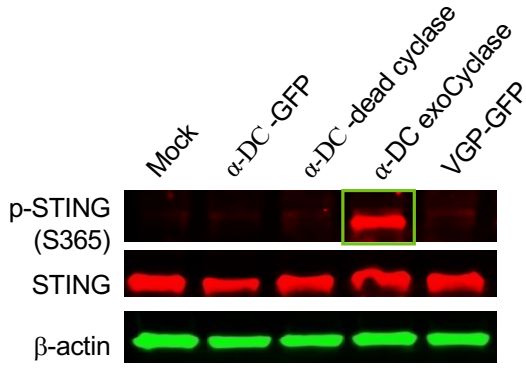
1. Esphera delivers STING agonism only to antigen presenting cells via the ExoGen immune-cell targeting domain
2. Esphera does not deliver small molecule; we deliver an enzyme that generates STING small molecule intracellularly (only in targeted cells)
3. To further safeguard against potential off-target events, Esphera uses bacterial cyclic dinucleotides are not efficiently taken up by effector immune cells



Engineered, Immunostimulatory Exosome



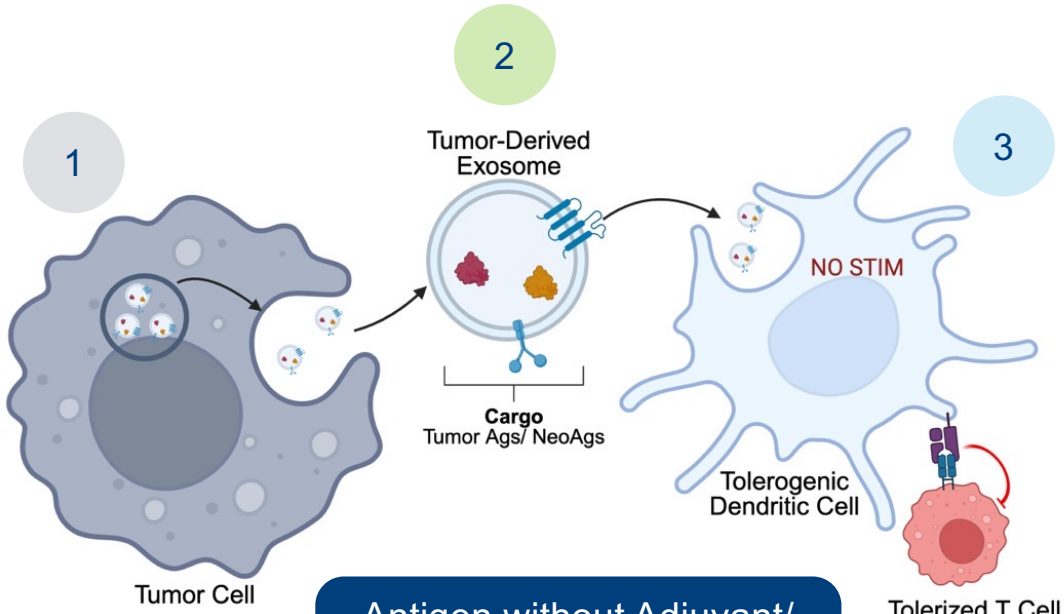
Intracellular generation of STING agonist



DC-targeted exosomes bearing bacterial cyclase activate STING

Tumor Cell Biology: Exosomes Tolerize the Immune System

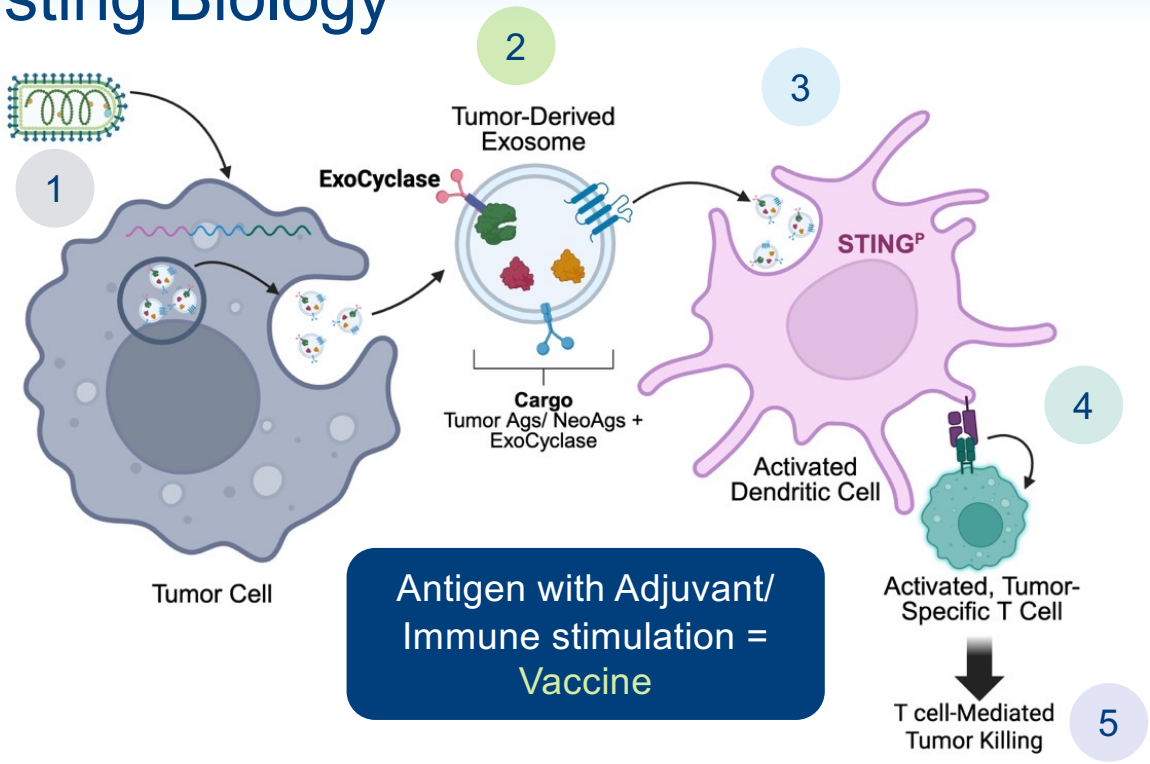
1	Tumor cells are known to be prolific producers of exosomes
2	Tumor-derived exosomes are known to contain tumor antigens (including neoAgs)
3	Tumor-derived exosomes are naturally immunosuppressive as they provide antigen without stimulation



Antigen without Adjuvant/ Immune stimulation = Tolerance

Esphera Hijacks Pre-Existing Biology

1	Delivery of Esphera's ExoCyclase transgene to tumor cells in vivo
2	ExoCyclase protein traffics to budding tumor-derived vesicles creating in vivo cancer vaccine
3	In vivo engineered nanomedicines deliver cyclase and tumor antigens to DCs
4	DCs produce STING agonist intra-cellularly, activating and maturing them to present tumor antigens to T-Cells
5	Activated T-Cells kill tumors cells



By capitalizing on the existing biology, we escape the need for tumor Ag prediction, achieving a personalized cancer vaccine with an off-the shelf drug.

OVs for Best-in-Class ExoCyclase Delivery to Tumors

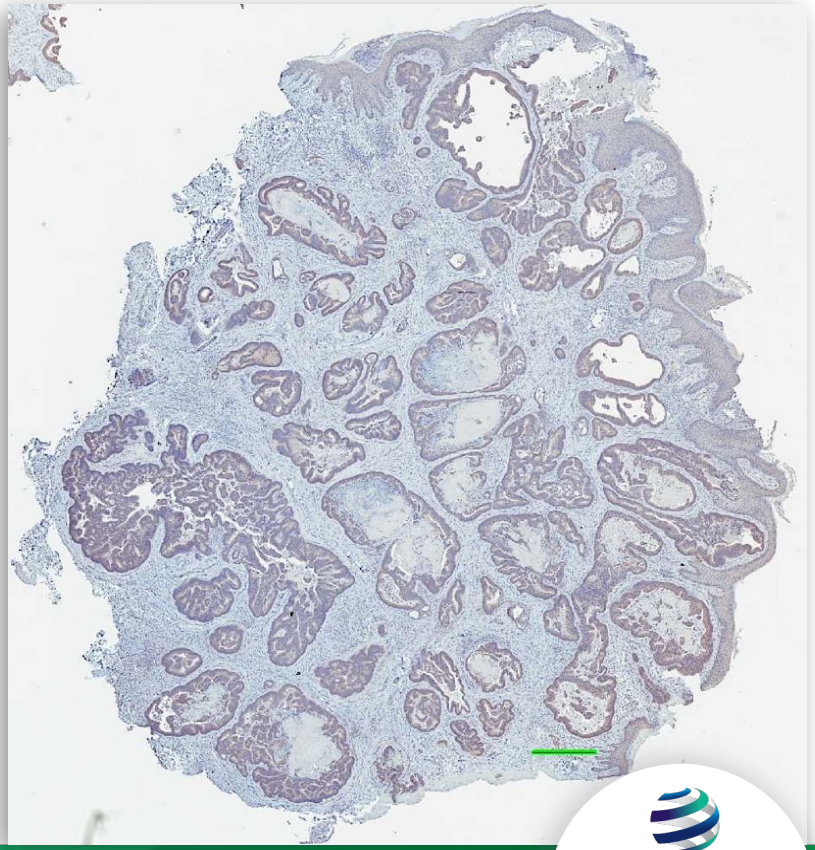
Oncolytic viruses represent the gold standard for transgene delivery to tumors, offering unmatched precision, safety and potency

Clinical and commercial feasibility

- ✓ Several trials have demonstrated successful transgene delivery following I.V. delivery

  nature Breitbach et al, 2011

- ✓ Long track record demonstrating clinical safety
- ✓ Esphera co-founders are the world-leading experts in manufacturing, scaling, and Phase I launch of OV trials
- ✓ Current manufacturing commercially feasible with excellent COGs



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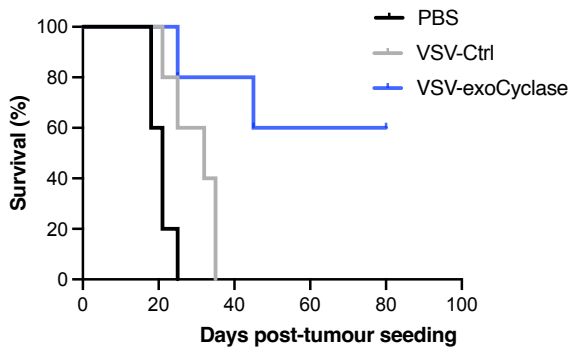
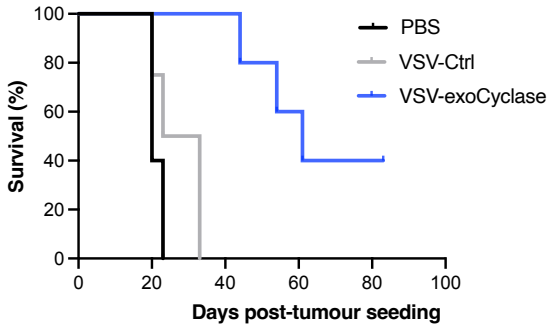
Curative Outcomes in Several Syngeneic Mouse Models

VSV-exoCyclase monotherapy leads to a significant anti-tumoral outcome in several mouse models of cancer

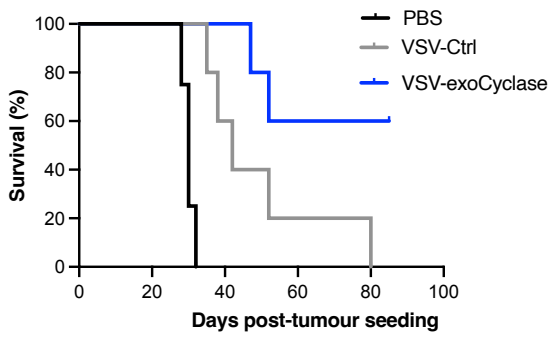
B16 Melanoma Cancer Model



MC38 Colorectal Cancer Model



KPL-3M NSCLC Model



Animals with established subcutaneous tumors were given 4 doses, starting on day 7

First in Class Oncology Opportunity

Ideal Cancer Vaccine Product Profile	
1	**Polyvalent.** To avoid immune escape mechanisms, the ideal tumor vaccine should be targeted to more than one antigen
2	**Personalized.** Effective tumor vaccines will include personalized tumor antigens
3	**Off-the-Shelf.** To ensure rapid patient availability, and cost-effective manufacturing, commercially viable cancer vaccines should be off-the-shelf
4	**Potent.** Vaccines must provide targeted co-delivery of both antigens and potent immune stimulation

Esphera's revolutionary approach to personalized cancer vaccines delivers on every front.

To the best of our knowledge, ESPH-01 is the first off-the-shelf and personalized polyvalent cancer vaccine

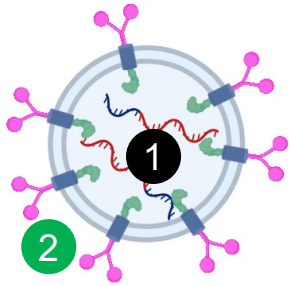
Significant R&D Progress Made Since Seed Financing

In addition to $2M CAD Seed financing (closed Oct 2023), Esphera has secured and leveraged an additional $5M CAD non-dilutive financing to advance the ExoGen platform, ESPH-01 lead asset and complete pivotal POC studies for additional pipeline opportunities.

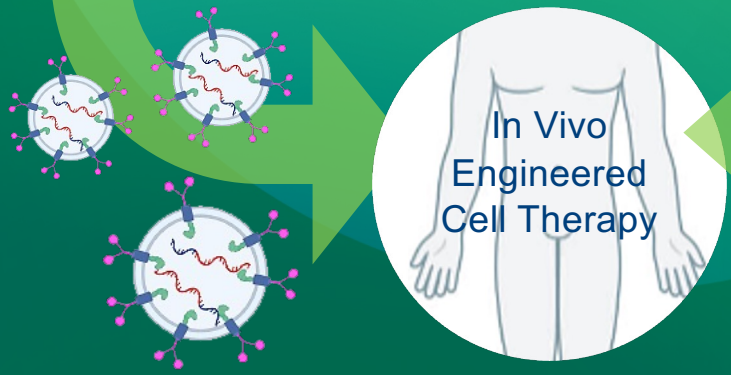
	In Vivo Engineering Asset Opportunities			
	Asset / Delivery Modality	Field	Milestones Achieved	Development Strategy
Oncology Pipeline	ESPH-01 Replicating Viral Vector	Oncology, Cancer Vaccine	In Vivo POC, Product lock, Manufacturing POC	Advance through Phase I clinical POC using Series A Proceeds
	ESPH-02 Enveloped Delivery Vehicle	Oncology, In vivo CAR-T	IP filed, Ex vivo POC	Advance through In Vivo POC then seek R&D collaboration/license
	Personalized Ag LNP/mRNA	Oncology, Cancer Vaccine	In vivo POC	Biotech/Pharma license deal
Infectious Disease	Target Ag TBD LNP/mRNA	Human Infectious Disease, Vaccine	In vivo POC, **Active Pharma R&D Collaboration**	Advance in partnership with Pharma, and out-license ahead of Phase I
	Target Ag TBD Non-replicating Viral Vector	Vet Infectious Disease, Vaccine	In vivo POC, Biotech R&D Collaboration, **NEW: Pharma NDA, R&D plan**	Advance in partnership with Pharma, and out-license ahead of Phase I

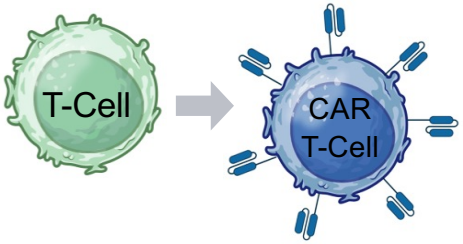
Esphera's In Vivo CAR T-Cell Technology Opportunity

Enveloped
Delivery Vehicle
(drug product)



1. Esphera's human T-Cell adapted saRNA encoding CAR transgene
2. ExoGen construct to enhance saRNA loading and T-Cell targeting/delivery





Circulating T-Cells take up engineered vesicle; saRNA generates strong and durable expression of functional CAR.

Technology delivers a human T-Cell-adapted saRNA to T-Cells causing strong and durable CAR expression using an off-the-shelf, lentivrus-free solution.

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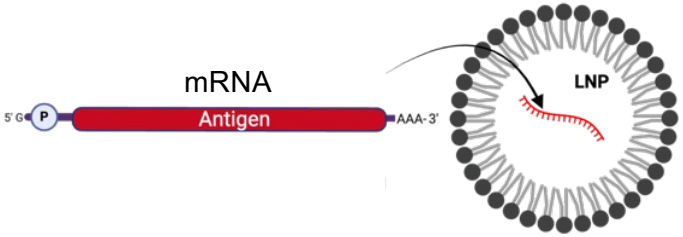
Drug Product Design for Step Change LNP/mRNA Vaccines

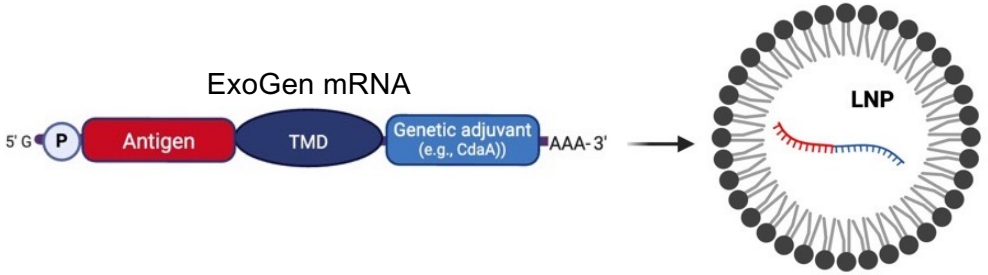
First Generation LNP/mRNA Vaccines



- ✓ Generate robust Ab responses in short term
- ✗ Immuno-stimulation provided by LNP – may not promote optimal T-Cell responses
- ✗ May not provide long-term memory responses in humans*

* Nguyen, D.C., Hentenaar, I.T., Morrison-Porter, A. et al. SARS-CoV-2-specific plasma cells are not durably established in the bone marrow long-lived compartment after mRNA vaccination. Nat Med 31, 235–244 (2025).

ExoCyclase LNP/mRNA Vaccines

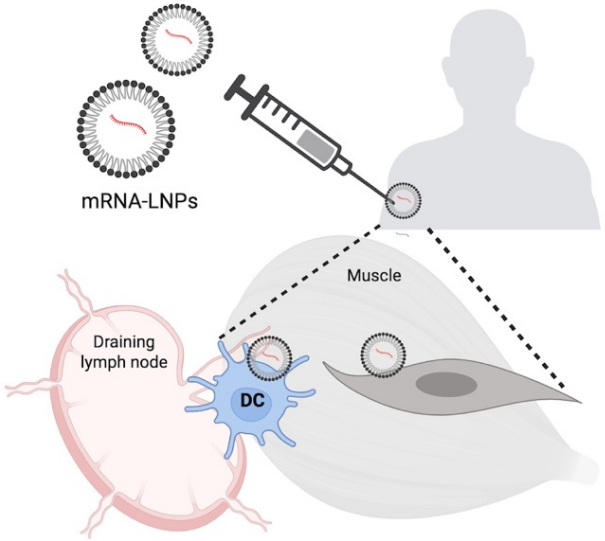


- ✓ Same manufacturing process, highly similar drug product, leads to enhanced immune responses simply modifying mRNA design
- ✓ In vivo engineered nanomedicines co-deliver Ag and strong adjuvant to immune cells leading to superior Ab and T-Cell responses
- ✓ Potential opportunity to dose down, reducing COGs

Esphera's Step-Change Opportunity for LNP/mRNA Vaccines

First Generation LNP/mRNA Vaccines

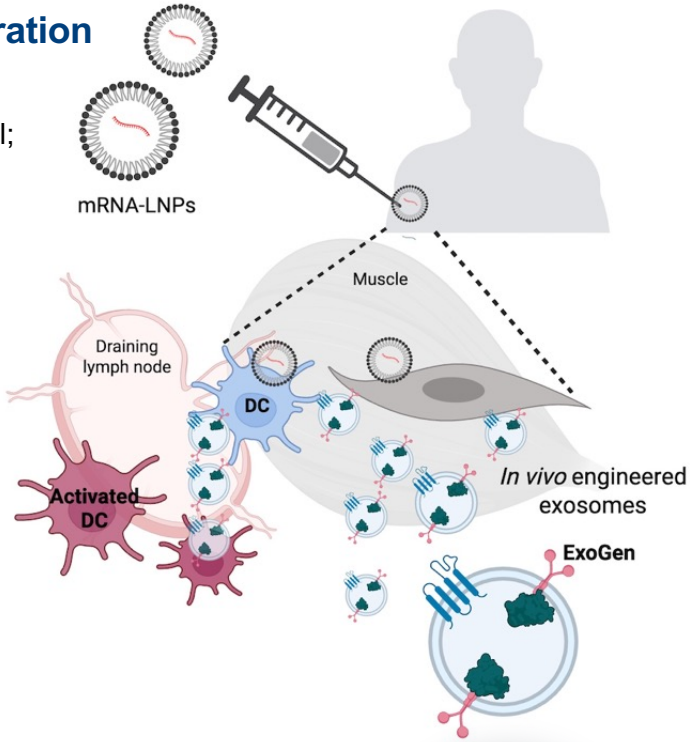
mRNAs released in cells produce vaccine Ag, and LNP stimulates recruitment of DCs for Ag presentation, and eventual neutralizing Ab responses.



Esphera's Next Generation LNP/mRNA Vaccines

Initial mechanism is identical; Esphera's vaccines will generate the same baseline immune responses as first generation vaccines.

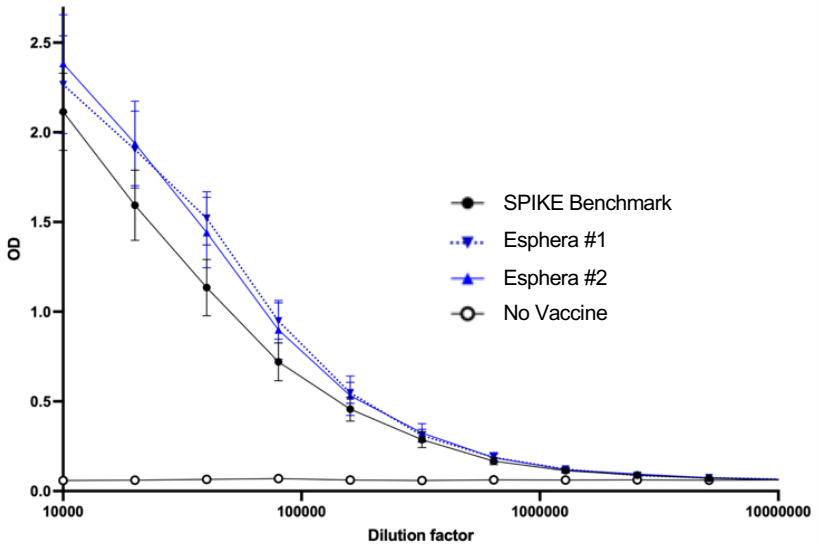
ExoGen delivery via LNP will then further amplify immune responses.



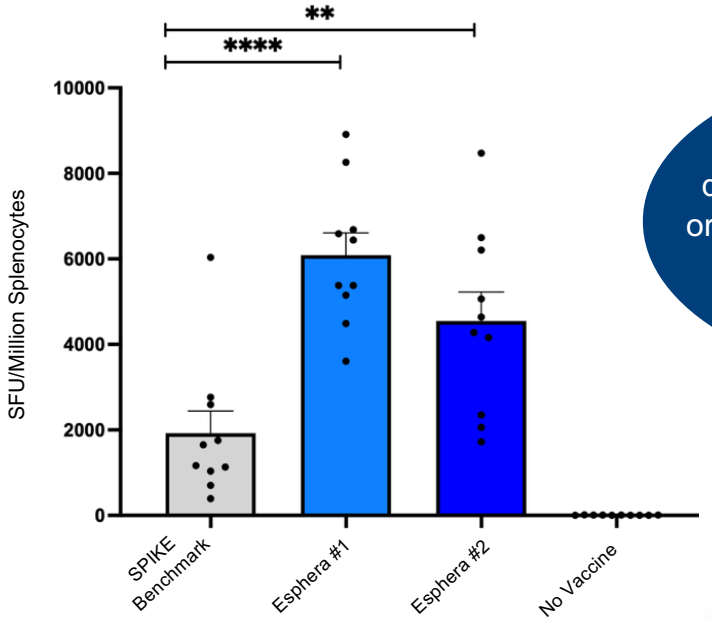
Esphera Enhanced LNP/mRNA Vaccine In Vivo POC

Esphera ExoCyclase LNP/mRNA has been compared to Moderna's COVID vaccine using standard dosing in mouse models

Neutralizing Antibody Titers

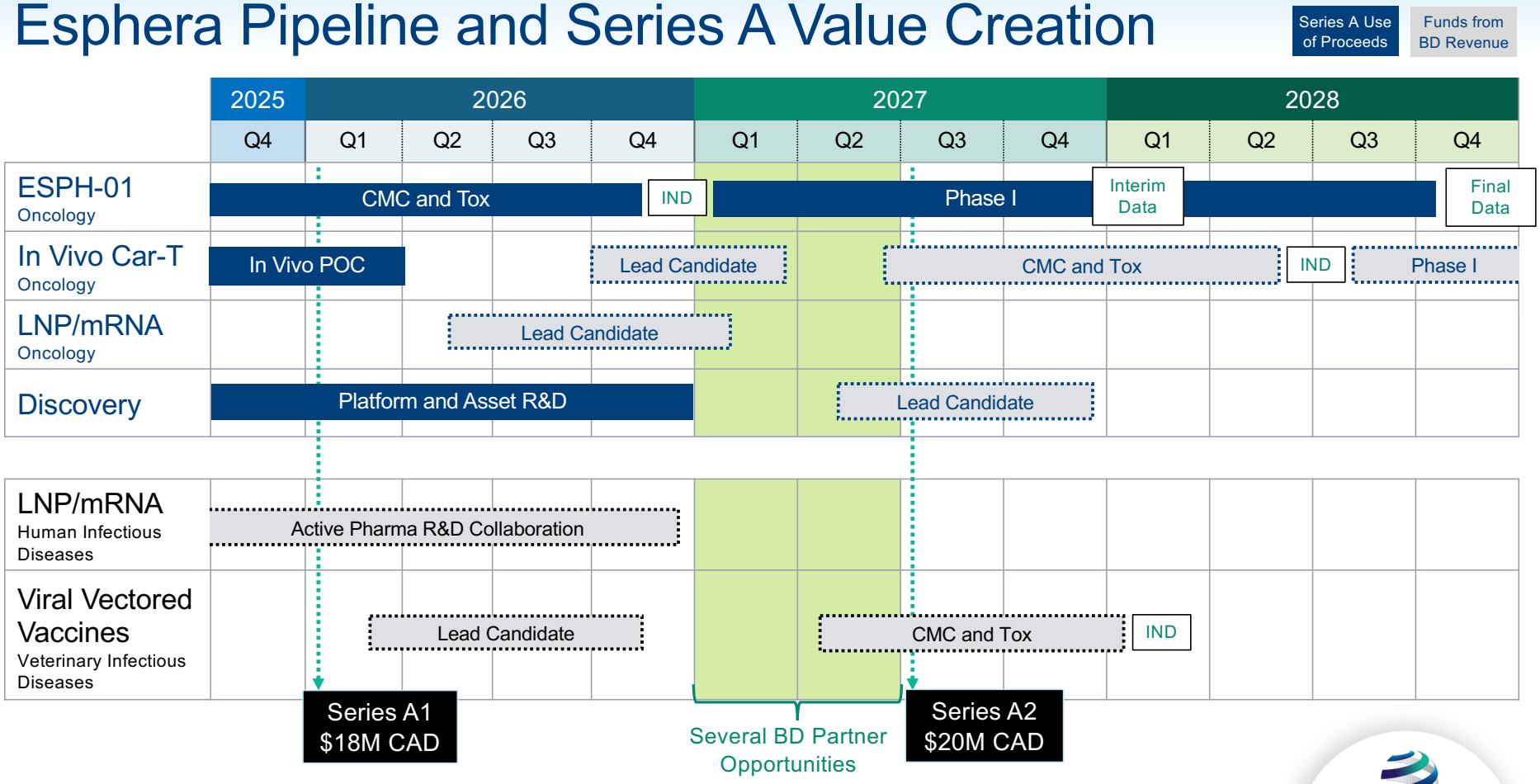


CD8 T-Cell Responses (ELISPOT)



Data consistently demonstrates equivalent or superior Ab responses, and significantly better T-Cell responses

Esphera Pipeline and Series A Value Creation



Financing Strategy and Next Steps

Esphera SynBio is seeking a Series A investment of $38M CAD

- Series A use of proceeds: ESPH-01 CMC, Tox, and Phase I clinical trial
- Pipeline applications to be funded through business development revenue and/or non-dilutive sources of capital

Why Invest

1. First-in-class lead asset oncology opportunity
2. Novel and proprietary solution to STING agonism
3. Significant pharma interest and additional licensing/exit opportunities:
    - Developing successful in vivo CAR T-Cell technology
    - Significantly improved immune responses for LNP/mRNA vaccines

Our Edge

- Pharma collaboration in infectious disease is underway
- Significant BD license opportunities in near-term
- Experienced team
- Strong track record raising non-dilutive capital to extend runway

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For more information:

Brian Lichty, CEO
blichty@EspheraSynbio.ca

Julia Pomoransky,
Business Development
jpomoransky@EspheraSynbio.ca